Advisory Action rendered September 26, 2002. Applicants respectfully request reconsideration of the Final Rejection and Advisory Action in light of the foregoing and the ensuing remarks.

The claims have been amended as follows: claim 7 has been amended to indicate that the language "from one to about three" refers to the Markush group following the phrase "oxygen-labile species", to delete the language "ascorbic acid derivatives" and "tocopherol derivatives and a mixture" and to add the language -wherein at least one of said oxygen-labile species is a retinoid- in order to clarify the claim language and to describe better certain embodiments of the invention. Basis for this amendment may be found in the Specification at page 4, line 30 through page 5, line 6.

Claim 17 has been amended to delete the following language: "ascorbic acid derivatives" and "tocopherol derivatives" and to add the articles -a- and -an- in order to clarify the language of the claim. Claim 18 has been amended in order to remove the clauses "and their derivatives" and "and mixtures thereof" and to add the clauses -at least one- and -or a combination of said water-soluble oxygen-labile species- in order to clarify the meaning of the claim. These amendments find basis in the Specification at page 4, line 30 through page 5, line 6 and in original claim 6.

Claims 19 and 20 have been amended in order to render them independent and incorporate the language of claim 7, the claim from which they formerly depended.

Claim 21 has been amended to clarify the term "antioxidants" by adding the language -other than said oxygen-labile species- in order to specify that additional antioxidants

may be utilized in the compositions of the invention, as set forth in the Specification at page 9, lines 5-11.

Claims 22-24 have been amended in order to clarify the amounts of different elements in the compositions of the invention. These amendments find basis in the Specification at page 2, line 26 through page 3, line 16.

A marked-up copy of the amended claims is appended hereto.

Applicants gratefully acknowledge the withdrawal of the objection to claim 1 and the withdrawal of the rejections of the claims under 35 U.S.C. §112, second paragraph and 35 U.S.C. §102. Applicants respectfully request reconsideration of these rejections in light of the foregoing amendments to the claims and the ensuing discussion.

The Final Rejection of May 6, 2002 set forth several rejections. Claims 7, 15, 17, 18 and 21 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regards as the invention.

Claims 7, 15, 17, 18 and 21 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This rejection was based on the use of a number of terms, including "derivatives", "from one to about three", "from about one to about three", "at least one stabilizer compound", "at least one retinoid", "at least one tocopherol" or "at least one ascorbic acid". Claims 7 and 18 were rejected as being indefinite based upon the use of the term "a mixture thereof". Claim 17 was deemed indefinite due to the use of the term "at least two oxygen-labile species". Claim 21 was rejected as indefinite due to the use of the term

"an antioxidant", the office action indicating that "it is unclear the oxygen-labile species and antioxidants are mutually exclusive" [Final Rejection, p. 4]. Claims 22-24 were found to be indefinite due to the use of the term "from about...to about".

Applicants respectfully request reconsideration of these rejections with respect to the amended claims in light of the ensuing discussion. Applicants have amended the claims to clarify their meaning, as follows: in order to clarify the term "derivatives", applicants now refer to the classes of compounds as currently set forth in claims 19 and 20, as a retinoid, an ascorbic acid and a tocopherol. Applicants have attempted to clarify the term "from one to about three" and like clauses, and have either clarified the object it is modifying or indicated that the composition contains "at least one" of the Markush group. Indeed, in certain embodiments, the composition may contain a retinoid and one or more of the listed species--the claims describes a genus to which such embodiments belong. Similarly, in claim 18, the language has been amended to describe embodiments where the composition of claim 7 may further contain at least one of the listed water-soluble oxygen-labile species in the Markush group or a combination of such species. Claims 22-24 have been amended to clarify the amounts of retinoid, tocopherol, ascorbic acid and/or N-acetyl cysteine are present in the described embodiments. Applicants respectfully submit that the foregoing amendments address the concerns set forth in the rejection of May 6, 2002 and request reconsideration thereof. Applicants respectfully reserve the right to file divisional applications relating to other embodiments of the inventions set forth in the above-captioned application.

In response to the comment set forth in the Advisory Action of September 26, 2002 as follows, applicants respectfully request reconsideration:

> Claim 22, for example, is indefinite because of the use of the term "of about 0.01 to about 10% for retinoid. The term "of about...to about" renders the claim indefinite. It is unclear the amount of retinoid is below 10% as to "to10%' or above 10%, as to "about 10%"...[Advisory Action, p. 2]

Applicants respectfully note that the MPEP permits the use of relative terminology and states that this term need not be considered indefinite: "Acceptability of the claim language depends on whether one of ordinary skill in the art would understand what is claimed, in light of the specification." [MPEP, §2173.05(b)]. Furthermore, the MPEP states that the term "about" may be used in certain cases, e.g., "because infringement could clearly be assessed..." [MPEP, §2173.05(b)(A)]. Thus, where the element may be measured, the term "about" is not considered indefinite under 35 U.S.C. §112. Therefore, in the claims as amended, the range of retinoid concentration in the compositions of applicants' invention may clearly be measured in relation to the weight of the composition. Further, one of ordinary skill in the art would clearly be able to measure retinoid concentration in an allegedly infringing product at either end of the range, whether the concentration is more or less than "about" 0.01% or 10%. Applicants respectfully request reconsideration of the rejections under 35 U.S.C. §112 in light of the amendments to the claims and the foregoing discussion.

The Final Rejection of May 6, 2002 further rendered several rejections under 35 U.S.C. 102(a) and (b). Applicants

respectfully request reconsideration of these rejections with respect to the amended claims in light of the ensuing discussion.

Claims 7, 15 and 21 were rejected under 35 U.S.C. 102(b) as being anticipated by Malfroy-Camine et al. (U.S. Patent No. 5,403,834) on the ground that Malfroy-Camine et al. "teach a pharmaceutical composition [containing] a salen-transition metal complex which can be administered alone or in combination with one or more free radical scavengers such as tocopherol, ascorbic acid and N-acetylcysteine..." [Final Rejection, p. 5]. Claims 7, 15 and 23 were also rejected under 35 U.S.C. 102(b) as being anticipated by Bland (U.S. Patent No. 5,637,324) on the basis that "Bland teaches a dietary composition comprising 0.05-0.25% by weigth of calcium ascorbate, 0.1-0.4% of D-α-tocopherol and 0.08-022% of N-acetylcysteine" [Final Rejection, p. 5]. Applicants respectfully request reconsideration of these rejections with respect to the amended claims and in light of the ensuing discussion.

Applicants have amended claims 7, 15, 21 and 23 to describe certain embodiments of their invention that contain a retinoid compound. Neither Malfroy-Camine et al. nor Bland teaches a composition that contains a retinoid. Applicants respectfully note that the proposed amendment to claim 23 in the Amendment Under 1.116 contained an inadvertent typographical error in line 3: the range of retinoid in the composition should have been indicated to be -from about 0.01% to about 10%- rather than "from about 0.0 to about 10%". Thus, the claims as amended describe embodiments of applicants' invention that would not be described or suggested by either the Malfroy-Camine et al. or Bland patents. Applicants therefore respectfully request

reconsideration of the rejections under 35 U.S.C. 102(b) in view of Malfroy-Camine et al. and Bland.

Claims 7, 15, 18 and 21 were rejected under 35 U.S.C. 102(a) as being anticipated by Cruz (U.S. Patent No. 5,843,481) on the basis that this patent "teaches a pharmaceutical composition comprising a vanadate compound...in combination with one or more antioxidants including ascorbic acid, α-tocopherol, N-acetylcysteine and a flavonoid, and effective amounts of the vanadate compound and the antioxidants are used..." [Final Rejection, p. 6]. Claims 7 and 15 were further rejected under 35 U.S.C. 102(a) as being anticipated by Fisher et al. (WO 98/55075) on the ground that "Fisher et al. teach a composition for ameliorating various effects of UV radiation comprising effective amounts of retinoid and antioxidants such as ascorbic acid and N-acetylcysteine..." [Final Rejection, p. 6]. Applicants respectfully request reconsideration of the foregoing rejections with respect to the amended claims and in light of the ensuing discussion.

As set forth above, the amended claims relate to embodiments containing at least a retinoid. Cruz does not suggest or describe compositions containing retinoids, therefore, it does not suggest or describe the embodiments of applicants' invention set forth in the claims as amended.

Fisher et al. relates to compositions and methods for inhibiting photoaging of human skin. While Fisher et al. mentions retinoids, ascorbic acid and N-acetylcysteine as potential MMP inhibitors, nowhere does it propose the formulations described by the amended claims. It merely lists these compounds as entities that can serve as MMP inhibitors for human skin. Thus, Fisher et al. does not suggest or describe the

compositions set forth in applicants' claims as amended. Applicants therefore respectfully request reconsideration of the rejections under 35 U.S.C. 102(a).

Applicants gratefully acknowledge the indication that claims 19 and 20 would be allowable if rewritten in independent form. Applicants have amended claims 19 and 20 in order to place them in better form for allowance and respectfully request their consideration as amended.

Applicants respectfully submit herewith a Request for Continued Examination and a Petition for Extension of Time. If there are any questions regarding this action, the Examiner is respectfully invited to contact the undersigned. An early allowance is earnestly solicited.

Respectfully submitted,

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APPENDIX - MARKED-UP COPY OF CLAIMS AS AMENDED

7. (Twice Amended) A composition comprising therapeutically active amounts of [from one to about three] a retinoid and from one to three oxygen-labile species selected from the group consisting of a retinoid[s], choleciferol, vitamin K, an ascorbic acid, [ascorbic acid derivatives,] a tocopherol [and tocopherol derivatives and a mixture thereof]; and a stabilizer compound comprising N-acetylcysteine.

17. (Twice Amended) A composition [according to claim 7] comprising a retinoid and at least two oxygen-labile species selected from the group consisting of choleciferol, vitamin K, an ascorbic acid, [ascorbic acid derivatives] and a tocopherol [and tocopherol derivatives]; and a stabilizer compound comprising N-acetylcysteine.

18. (Twice Amended) A composition according to claim 7 wherein said composition further comprises [a] at least one water-soluble oxygen-labile species selected from the group consisting of niacin, thiamine, riboflavin, folic acid, pyrodoxine, pantothenic acid, niacinamide, lipoic acid, dihydroplipoic acid, and an amino acid [and mixtures thereof].

19. (Twice Amended) A composition [according to claim 7] comprising therapeutically active amounts of at least one oxygen-labile species selected from the group consisting of a retinoid, choleciferol, vitamin K, an ascorbic acid, [ascorbic acid derivatives,] and a tocopherol; and a stabilizer compound

comprising N-acetylcysteine wherein said oxygen-labile species are a retinoid, a tocopherol and an ascorbic acid.

21. (Amended) A composition according to claim 7 wherein said composition further comprises a humectant, an antioxidant other than said oxygen-labile species, a preservative, a fragrance, a surface active agent, a binder and a skin protectant agent.

22. (Amended) A composition comprising a retinoid in an amount of [from] about 0.01% to about 10% by weight of the composition [of a retinoid], a tocopherol in an amount of [from] about 0.01% to about 10% by weight of the composition [of a tocopherol] and an ascorbic acid in an amount of [from] about 0.01% to about 20% by weight of the composition [an ascorbic acid] N-acetylcysteine in an amount of [and from] about 0.001% to about 5% by weight of the composition [of N-acetylcysteine].

23. (Twice Amended) A composition [according to claim 7] comprising an ascorbic acid in an amount of [from] about 0.01% to about 5% by weight of the composition [of ascorbic acid], a retinoid in the amount of from about 0.01% to about 10% by weight of the composition and N-acetylcysteine in an amount of [from] about 0.001% to about 0.1% by weight of the composition [of N-acetylcysteine].

24. (Amended) A composition comprising an ascorbic acid in an amount of [from] about 0.01% to about 5% by weight of thecomposition [of ascorbic acid], a tocopherol in an amount of [from] about 0.01% to about 1% by weight of the composition [of tocopherol] and retinol in an amount of [from] about 0.01% to

about 0.4% by weight of the composition [of retinol] and N-acetylcysteine in an amount of [from] about 0.01% to about 0.1% by weight of the composition [of N-acetylceysteine].